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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,361	06/20/2003	Jean-Marie Andrieu	1187-R-02	7112

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IP GROUP OF DLA PIPER LLP (US)
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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
11/06/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pto.phil@dlapiper.com

Office Action Summary	Application No.	Applicant(s)	
	10/600,361	ANDRIEU ET AL.	
	Examiner	Art Unit	
	EMILY M. LE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44 and 52-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44 and 52-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/11/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/11/2009 has been entered.

Status of Claims

2. Claims 1-43, 45-51 are cancelled. Claims 44 and 52-56 are pending and under examination.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Belardelli et al.[1]

In response to the rejection, Applicant argues that the claimed invention is not obvious over the Belardelli et al. To support Applicant's position, Applicant argues that Belardelli et al. is non-analogous art because it deals with preventative vaccines,

[1] Belardelli et al. U.S. PreGrant Patent No. 2003/0092177 A1, filed April 27, 2001.

whereas the claimed invention deals with therapeutic vaccines. Applicant also argues that one of ordinary skill in the art would not be motivated by Belardelli et al. to attempt the preparation of a therapeutic vaccine comprising autologous dendritic cells and autologous HIV because one of ordinary skill in the art would never, on the basis of the disclosure of Belardelli et al., use autologous HIV in combination with autologous dendritic cells to prepare a therapeutic vaccine. Applicant additionally argues that one of ordinary skill in the art would have had no indication of what type of virus to include in a therapeutic vaccine.

Applicant's argument has been considered, however, it is not found persuasive. In response to applicant's argument that Belardelli et al. is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Belardelli et al. is in Applicant's field of endeavor. Applicant's claimed invention is directed to a composition comprising autologous dendritic cells pulsed/loaded with an inactivated autologous antigen. Belardelli et al. teaches a composition comprising autologous dendritic cells pulsed with an inactivated antigen. The only difference between the two compositions is that the composition of Belardelli et al. does not comprise an inactivated autologous antigen. However, it remains that both the claimed composition and the composition of Belardelli et al. comprises autologous dendritic cells pulsed with an antigen. Belardelli et al. is in the field of Applicant's endeavor.

Additionally, it is noted that Applicant has mischaracterized the teachings of Belardelli et al. as limited to preventative vaccines. In the abstract, Belardelli et al. clearly sets forth that the composition can be used for therapeutic purposes.

Additionally, contrary to Applicant's assertion that one of ordinary skill in the art would not be motivated by Belardelli et al to attempt the preparation of a therapeutic vaccine comprising autologous dendritic cells and autologous HIV because one of ordinary skill in the art would never use autologous HIV in combination with autologous dendritic cells to prepare a therapeutic vaccine; Belardelli et al. clearly teaches a composition comprising autologous dendritic cells pulsed with an inactivated antigen, wherein one of the antigen taught by Belardelli et al. is an inactivated HIV as the antigen. And, in at least the abstract, Belardelli et al. teaches the use of such composition for therapeutic purposes, as a therapeutic composition.

While Belardelli et al. did not specifically suggest an inactivated autologous HIV antigen; KSR forecloses the argument that specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR*, 82 USPQ2d at 1396. As noted, Belardelli et al. teaches the use of an inactivated HIV antigen. In the instant case, Belardelli et al. clearly teaches the use of an inactivated HIV antigen. Belardelli et al. also teaches of patient-specific therapy with the use of autologous dendritic cells. One of ordinary skill in the art, at the time the invention was made reading Belardelli et al., along with the knowledge in the art at there are many variability in the many type of HIV isolates and the ability of the virus to mutate, would clearly be motivated by Belardelli et

al. to use an inactivated HIV antigen, including inactivated autologous HIV antigen to induce an immune response against the specific HIV isolate infecting the subject.

In addition to above, Applicant criticizes the Office as being divorced from reality for noting that there is great genetic variation among the many different types of known HIV isolates due to the propensity of the virus to mutate. Applicant notes that Applicant's use an autologous HIV was not haphazard, accidental decision based on the propensity of the virus to mutate or the high degree of variability among the different HIV virus.

Applicant's criticism is noted. The Office is not asserting that Applicant's use of autologous HIV antigen was a haphazard, accidental decision based on the propensity of the virus to mutate or the high degree of variability among the different HIV virus. However, the Office has clearly set forth in the record that due to the noted variability, combined with the teachings of Belardelli et al., it would have been prima facie obvious for one of ordinary skill in the art to use an inactivated autologous HIV antigen.

Applicant further argues that over nearly three decades, no other research team other than Applicant's has demonstrated the physical destruction of CD4+ lymphocytes super-infected by the HIV virus. To support Applicant's argument, Applicant specifically cited Figure 3.

Applicant's argument has been considered, along with Figure 3, however, it is not found persuasive. According to Applicant's specification, HIV-gag-specific B-LCL killing was up-regulated by autologous PBL stimulated with autologous virus-pulsed dendritic cells. Applicant also noted that the CTL-meditated B-LCL killing was executed

exclusively by CD8+ T cells. In the instant case, Applicant contributes the killing to CD8+ T cells. At the time the invention was made, Belardelli et al. establishes that dendritic cells disclosed therein are capable for use in expansion of T cells, including CD8+. [Paragraphs 0013 and 0045, in particular.] Thus, while the Office appreciates Applicant's discovery, however, as evidenced by the art, such discovery is clearly predicted and expected in the art.

In addition to above, it is noted that Applicant criticizes that the office appears to incorrectly rely on argument which conflate anticipation and anticipated related doctrines with obviousness and obviousness related doctrines. Applicant specifically refers to the content on page 8 of the previous office action. Applicant also criticizes the Office for noting that the composition of Belardelli et al. is "the same as instantly claimed".

Applicant's criticisms have been noted. It should be further noted that it is clear on the record that the instant rejection is an obviousness rejection. Had the cited reference teaches every limitation of the claimed invention, the Office would have readily cited the reference as anticipating the claimed invention. However, as in this case, the Office cited the reference as rendering the claimed invention obvious. The comment made on page 8 of the previous office action is directed to the functional language recited in the claims. The claims requires that the compositions expands in vivo expression of virus-specific CD8+ T cells, and said virus-specific CD8+ cells kill HIV-infected cells. In the instant case, Belardelli et al. teaches a composition comprising autologous dendritic cells pulsed with inactivated HIV virus. The difference is that the

inactivated HIV virus of Belardelli et al. is not an autologous HIV virus, **to clarify the record**. However, the compositions of the claimed invention and that of Belardelli et al. comprise two main ingredients, autologous dendritic cells and inactivated HIV virus. Among the two main ingredients, Belardelli et al. teaches that the dendritic cells can be used for the expansion of T cells, including CD8+. [Paragraphs 0013 and 0045, in particular.] In the instant case, Belardelli et al. clearly sets forth that dendritic cells are capable of expanding CD8+ cells, an inherent feature of dendritic cells.

As presented in the 12/19/08 office action, the claims are directed to a composition comprising dendritic cells pulsed with an inactivated human immunodeficiency virus (HIV), wherein the dendritic cells are obtained from a monocyte by plastic-adherence followed by culture with GM-CSF and IL-4 and a pharmaceutically acceptable carrier, requires that the virus be autologous and wherein the virus is chemically inactivated by 2,2'-dithiopyridine. Additionally, the claims require that the virus be isolated from the blood tissue of the patient, and that composition be obtained by isolating peripheral blood mononuclear cells from whole blood, subjecting the peripheral blood mononuclear cells to plastic adherence, culturing the adherent cells with GM-CSF and IL-4 to obtain the dendritic cells, adding to 2,2'-dithiopyridine-inactivated virus to the dendritic cells and culturing the cells.

Belardelli et al. teaches composition comprising dendritic cells pulsed with an inactivated human immunodeficiency virus (HIV) and a pharmaceutically acceptable carrier. [Paragraphs 0066-0067 and 0071, in particular.] The dendritic cells used by Belardelli et al. were obtained from a monocyte by plastic-adherence followed by culture

with GM-CSF and IL-4. Belardelli et al. uses AT-2, 2,2'-dithiopyridine, to chemically inactivate the virus. And Belardelli et al. uses autologous dendritic cells.

While the dendritic cells used by Belardelli et al. are autologous, it is not readily apparent if the virus used by Belardelli et al. is also autologous. It should be noted that Belardelli et al. uses the cells as an adjuvant, and the inactivated virus as an immunogen/antigen.

However, due to the many variability in the many type of HIV isolates and the ability of the virus to mutate, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to use autologous HIV. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to induce an immune response against the specific HIV isolate infecting the subject. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the use of autologous antigens is routinely practiced in the art.

It is noted that the claims require the composition to expands in vivo expression of virus-specific CD8+ T cells, and said virus-specific CD8+ cells kill HIV-infected cells; however, MPEP § 2112 [R-3] (I) provides: [T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re

Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." Id.

In the instant case, while it may be true that Applicant discovers that the claimed composition expands *in vivo* expression of virus-specific CD8+ T cells, and said virus-specific CD8+ cells kill HIV-infected cells; however, this discovery does not make the composition patentable over the composition of Belardelli et al. Belardelli et al. teaches a composition that is the same as instantly claimed. The composition of Belardelli et al. is the claimed composition. Hence, Belardelli et al. does not need to teach that the composition expands *in vivo* expression of virus-specific CD8+ T cells, and said virus-specific CD8+ cells kill HIV-infected cells to anticipate the claimed invention. The composition of Belardelli et al. would have the same properties or functions recognized by Applicant.

Regarding the process by which the claimed product is made, it should be noted that even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is

unpatentable even though the prior product was made by a different process." MPEP 2113, In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

5. Claims 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belardelli et al., as applied above to claim 44, in view of Lu et al.[2]

In response to the rejection, Applicant submits the arguments presented above, and adds that Lu et al. fails to cure the deficiencies of Belardelli et al.

Applicant's argument has been considered, however, it is not found persuasive for reasons discussed in paragraph 3 of this office action. And, contrary to Applicant's assertion, while the composition of Belardelli et al. does not further comprise indinavir, Lu et al. teaches that indinavir direct up-regulate proliferation and down regulate apoptosis of T cells. [Paragraph bridging pages 247-248.] In the instant case, Lu et al., together with Belardelli et al. renders the rejected claims obvious.

As presented in the 12/19/08 office action, the claims require the composition to further comprise an adjuvant. The adjuvant is later limited to a protease inhibitor by claim 53, which depends on claim 52. The protease inhibitor is later limited indinavir by claim 54, which depends on claim 53. Claim 55, which depends on claim 54, later requires that the composition comprise a non-antiviral concentration of indinavir. And claim 56 limits the non-antiviral concentration to 10 nM.

The significance of Belardelli et al., as applied to claim 43, is provided above.

[2] Lu et al. HIV protease inhibitors restore impaired T-cell proliferative response in vivo and in vitro: a viral-suppression-independent mechanism. Blood, Jul 2000; Vol. 96, 250 - 258.

The composition of Belardelli et al. does not further comprise indinavir. However, Lu et al. teaches that indinavir direct up-regulate proliferation and down regulate apoptosis of T cells. [Paragraph bridging pages 247-248.]

Thus, would have been prima facie obvious for one of ordinary skill in the art to combine the teachings of Belardelli et al. and Lu et al. One of ordinary skill in the art would have been motivated to do so to optimize CTL response against HIV infection. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the determination of a workable or optimal range is routinely practiced in the art.

It is recognized that claims require the composition to contain non-antiviral concentration of indinavir, specifically 10 nM. In the instant, Lu et al. teaches that the extent in which indinavir up-regulate proliferation and down regulate apoptosis of T cells varies at different concentrations of indinavir. Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use any concentrations of indinavir, particularly since Lu et al. establishes that indinavir at various concentrations, ranging from .1nM to 1000 nM, stimulates direct up-regulate proliferation and down regulate apoptosis of T cells. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to determine the optimum concentration to optimize the proliferation of T cells. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the determination of workable ranges or optimal value is routine practiced in the art.

Conclusion

6. No claims are allowed.

7. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to EMILY M. LE whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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